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The Epidemiology of Necrotizing Enterocolitis Infant Mortality in the United States

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Introduction

Necrotizing enterocolitis is the most common condition for which emergency gastrointestinal surgery is required during the neonatal period and an important cause of both morbidity and mortality in the preterm infant.¹⁻⁴ Despite extensive epidemiological, clinical, and basic research, the cause of necrotizing enterocolitis remains unproven. It is generally accepted that prematurity places the newborn at substantially increased risk for the condition,³ and increased case rates are associated with decreasing birthweight and gestational age.⁴ Moreover, necrotizing enterocolitis is unusual in the first few days of life and is primarily a disease of preterm infants who have survived the immediate neonatal period. Recent advances in neonatal intensive care have led to increased survival of smaller, more immature infants, who are at greatest risk for necrotizing enterocolitis.

In 1989, analysis of US death certificate data showed that annual infant mortality rates for necrotizing enterocolitis decreased from 14.5 deaths per 100 000 live births in 1979 to 10.2 deaths per 100 000 live births in 1985.⁵ Since 1985, both neonatal and infant mortality rates have declined.⁶ The introduction of exogenous surfactant in the early 1990s has been associated with a decrease in mortality among low-birthweight (<2500 g) infants.⁷ The present study was undertaken to describe current trends in infant mortality associated with necrotizing enterocolitis, to evaluate selected infant and parental characteristics that may be associated with necrotizing enterocolitis death, and to compare necrotizing enterocolitis

infant mortality rates in the pre- and post-surfactant eras.

Methods

Multiple cause-of-death and natality data for 1979 through 1992 and linked data for births and infant deaths for 1983 through 1991 were obtained from the National Center for Health Statistics, Centers for Disease Control and Prevention.⁸⁻²² On the basis of the ninth revision of the *International Classification of Diseases* (ICD),²³ necrotizing enterocolitis infant (<1 year of age) deaths were defined as deaths for which ICD-9 code 777.5 was recorded anywhere on the death certificate.

The multiple cause-of-death and natality¹⁰ data were used to determine the number of necrotizing enterocolitis deaths and annual infant mortality rates. Necrotizing enterocolitis infant mortality rates, calculated as the number of deaths per 100 000 live births, were determined overall and by race, sex, and standard region. The neonatal period was defined as less

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ABSTRACT

Objectives. This study examined trends and risk factors for infant mortality associated with necrotizing enterocolitis in the United States.

Methods. Necrotizing enterocolitis-associated deaths and infant mortality rates from 1979 through 1992 were determined by means of US multiple cause-of-death and linked birth/infant death data.

Results. Annual necrotizing enterocolitis infant mortality rates decreased from 1979 through 1986 but increased thereafter and were lower during the 3-year period before (1983 through 1985; 11.5 per 100 000 live births) the introduction of surfactants than after (1990 through 1992; 12.3 per 100 000). Low-birthweight singleton infants who were Black, male, or born to mothers younger than 17 had increased risk for necrotizing enterocolitis-associated death.

Conclusions. As mortality among low-birthweight infants continues to decline and smaller newborns survive early causes of death, necrotizing enterocolitis-associated infant mortality may increase. (*Am J Public Health*. 1997;87:2026-2031)

than 28 days of life. The periods 1983 through 1985 and 1990 through 1992 were compared because they represent periods before and after the widespread introduction of exogenous surfactant.^{24,25}

To examine infant characteristics that may be associated with necrotizing enterocolitis death, we analyzed the 1990 through 1991 linked birth/infant death data.^{18,19} Because necrotizing enterocolitis deaths are more frequent among low-birthweight infants,¹ this analysis concentrated on necrotizing enterocolitis deaths among low-birthweight singleton infants (10 with unknown weight were excluded). Multiple-birth infants ($n = 157$) were excluded from this analysis because of their known increased risk for prematurity.²⁶ Necrotizing enterocolitis infant mortality rates for low-birthweight singleton infants were calculated as the number of necrotizing enterocolitis low-birthweight singleton infant deaths per 100 000 low-birthweight singleton live births; rates for normal-birthweight (≥ 2500 g) singleton infants were based on the number of necrotizing enterocolitis normal-birthweight singleton infants per 100 000 normal-birthweight live births. Because some variables were not reported by all states, analyses for each variable were restricted to reporting states.¹²⁻²⁰

To further evaluate selected infant and parental characteristics, low-birthweight singleton necrotizing enterocolitis deaths were compared with low-birthweight singleton survivors. The following characteristics among infants were evaluated: race, sex, birthweight, gestational age, Apgar scores, live birth order in the family, and geographic region of birth. Birthweight was grouped as under 750 g, 750 through 999 g, 1000 through 1499 g, 1500 through 1999 g, 2000 through 2499 g, and 2500 g or more. The following maternal characteristics were evaluated: age, race, education, prenatal visits, trimester that care began, and marital status. Age and education of the father were also analyzed.

Crude and adjusted estimated relative risks with 95% confidence intervals were calculated by means of logistic regression analysis.²⁷ For linked birth/infant death analyses of low-birthweight singleton infants, necrotizing enterocolitis-associated deaths were compared with surviving infants. Birthweight-adjusted relative risks with 95% confidence intervals were first estimated with use of the low-birthweight categories noted above to control for birthweight. Statistically significant variables associated with necrotizing enterocolitis death (with birthweight and fully reported variables taken into account) were further

TABLE 1—Infant Mortality Rates for Necrotizing Enterocolitis: United States, 1983 through 1985 and 1990 through 1992

| | 1983–1985 | | 1990–1992 | | 1990–92/1983–85 | |
|--------------|-------------------|------|-------------------|------|-----------------|----------|
| | Rate ^a | No. | Rate ^a | No. | RR | 95% CI |
| Total | 11.5 | 1271 | 12.3 | 1515 | 1.1 | 1.0, 1.2 |
| Race | | | | | | |
| White | 8.1 | 718 | 8.0 | 760 | 1.0 | 0.9, 1.1 |
| Black | 28.9 | 517 | 33.2 | 720 | 1.1 | 1.0, 1.3 |
| Other | 7.8 | 36 | 5.5 | 35 | 0.7 | 0.4, 1.1 |
| Sex | | | | | | |
| Male | 13.0 | 740 | 13.7 | 867 | 1.1 | 1.0, 1.2 |
| Female | 9.8 | 531 | 10.8 | 648 | 1.1 | 1.0, 1.2 |
| Race and sex | | | | | | |
| White male | 9.7 | 441 | 9.1 | 447 | 0.9 | 0.8, 1.1 |
| White female | 6.5 | 277 | 6.7 | 313 | 1.0 | 0.9, 1.2 |
| Black male | 30.7 | 278 | 36.6 | 403 | 1.2 | 1.0, 1.4 |
| Black female | 27.1 | 239 | 29.7 | 317 | 1.1 | 0.9, 1.3 |
| Other male | 8.9 | 21 | 5.2 | 17 | 0.6 | 0.3, 1.1 |
| Other female | 6.7 | 15 | 5.8 | 18 | 0.9 | 0.9, 1.7 |
| Region | | | | | | |
| Midwest | 9.3 | 252 | 12.3 | 343 | 1.3 | 1.1, 1.6 |
| Northeast | 11.1 | 229 | 12.1 | 283 | 1.1 | 0.9, 1.3 |
| South | 14.5 | 555 | 15.1 | 633 | 1.0 | 0.9, 1.2 |
| West | 9.5 | 235 | 8.5 | 256 | 0.9 | 0.7, 1.1 |

Note. RR = relative risk; CI = confidence interval.

^aNecrotizing enterocolitis infant mortality rate expressed as necrotizing enterocolitis deaths per 100 000 live births; rates for pre-surfactant (1983 through 1985) and post-surfactant (1990 through 1992) periods.

analyzed by fitting a series of hierarchical logistic models and also by stepwise logistic regression. Multiple logistic regression analysis was performed with and without gestational period in the model.

Results

Multiple Cause-of-Death Data

From 1979 through 1992, 6629 necrotizing enterocolitis infant deaths were recorded, of which 80% had the condition listed as the underlying cause. Most necrotizing enterocolitis deaths (87%) occurred during the neonatal period. The average annual necrotizing enterocolitis infant mortality rate was 12.4 deaths per 100 000 live births, and an average of 474 infants died with the condition each year. The rate increased from 11.5 deaths per 100 000 live births during the pre-surfactant era to 12.3 deaths per 100 000 live births during the post-surfactant era (Table 1).

The necrotizing enterocolitis infant mortality rate for Black infants increased over time, whereas that for White and other-race infants did not (Table 1). From 1990 through 1992, the rate was more than four times as great for Black as for White

infants, although 50% of the deaths were among White infants. The necrotizing enterocolitis infant mortality rate was higher for males than females, and rates for both males and females were higher in 1990 through 1992 than in 1983 through 1985. When race and sex were evaluated together, rates for both male and female Black infants were higher in 1990 through 1992 than in 1983 through 1985. The South had the highest necrotizing enterocolitis infant mortality rate, accounting for 42% of necrotizing enterocolitis deaths in 1990 through 1992. Mortality rates for all regions, except the West, were higher in 1990 through 1992 than in earlier years. Compared with rates during 1983 through 1985, infant mortality rates for Blacks during 1990 through 1992 were higher in all regions, whereas those for Whites were higher in the Northeast and Midwest.

The distribution of other causes of death listed on the death record suggests that less mature infants were more likely to die with necrotizing enterocolitis in the later period. The categories "extreme immaturity" (ICD-9 765.0) and "other preterm infants" (ICD-9 765.1) were included on the records of substantially more necrotizing enterocolitis deaths in the later period than in 1983 through 1985 (22% vs 14% and 50% vs 44%, respectively).

TABLE 2—Infant, Maternal, and Paternal Characteristics of Low-Birthweight Singleton Necrotizing Enterocolitis Infant Deaths and Low-Birthweight Singleton Surviving Infants: United States, 1990 and 1991

| | Infant Mortality Rate ^a | Necrotizing Enterocolitis Deaths | | Surviving Infants | | Birthweight-Adjusted RR (95% CI) ^b |
|---------------------------------|------------------------------------|----------------------------------|------|-------------------|------|---|
| | | No. | % | No. | % | |
| Total | 159.1 | 764 | 100 | 444 742 | 100 | |
| Infant risk factors | | | | | | |
| Race ^c | | | | | | |
| White | 120.1 | 352 | 46.1 | 272 661 | 61.3 | Referent |
| Black | 235.0 | 386 | 50.5 | 150 632 | 33.9 | 1.5 (1.3, 1.8) |
| Other | 114.2 | 26 | 3.4 | 21 449 | 4.8 | 1.0 (0.7, 1.6) |
| Sex ^c | | | | | | |
| Male | 197.9 | 450 | 58.9 | 207 679 | 46.7 | 1.6 (1.4, 1.8) |
| Female | 124.2 | 314 | 41.1 | 237 063 | 53.3 | Referent |
| Region | | | | | | |
| Midwest | 167.0 | 176 | 23.1 | 97 041 | 21.8 | 1.0 (0.8, 1.3) |
| Northeast | 159.4 | 145 | 19.0 | 84 164 | 18.9 | 1.1 (0.9, 1.4) |
| South | 165.0 | 305 | 40.0 | 171 371 | 38.6 | 1.1 (0.9, 1.3) |
| West | 139.0 | 137 | 18.0 | 91 815 | 20.7 | Referent |
| Birthweight, g ^c | | | | | | |
| <750 | 689.5 | 168 | 22.0 | 7 076 | 1.6 | 114.4 (85.6, 153.0) |
| 750–999 | 914.8 | 165 | 21.6 | 13 669 | 3.1 | 58.2 (43.5, 77.8) |
| 1000–1499 | 555.5 | 238 | 31.2 | 38 663 | 8.7 | 29.7 (22.5, 39.2) |
| 1500–1999 | 151.7 | 130 | 17.0 | 81 722 | 18.4 | 7.7 (5.7, 10.4) |
| 2000–2499 | 20.4 | 63 | 8.2 | 303 612 | 68.3 | Referent |
| Gestational period, wk | | | | | | |
| <27 | 722.0 | 259 | 34.5 | 17 370 | 4.0 | 3.7 (2.7, 5.1) |
| 27–33 | 332.7 | 391 | 52.1 | 109 059 | 24.9 | 2.7 (2.1, 3.5) |
| ≥34 | 31.4 | 100 | 13.3 | 311 566 | 71.1 | Referent |
| 1-min Apgar score ^d | | | | | | |
| 0–3 | 366.7 | 165 | 30.0 | 26 832 | 7.7 | 1.3 (1.0, 1.7) |
| 4–7 | 261.6 | 291 | 49.3 | 104 691 | 30.2 | 1.4 (1.1, 1.8) |
| 8–10 | 61.3 | 134 | 22.7 | 215 642 | 62.1 | Referent |
| 5-min Apgar score ^d | | | | | | |
| 0–3 | 208.0 | 36 | 6.1 | 4 068 | 1.2 | 1.0 (0.7, 1.4) |
| 4–7 | 465.2 | 236 | 40.1 | 42 633 | 12.3 | 1.2 (1.0, 1.5) |
| 8–10 | 103.1 | 316 | 53.7 | 300 432 | 86.5 | Referent |
| Live birth order | | | | | | |
| 1st | 148.6 | 327 | 43.4 | 204 858 | 46.4 | Referent |
| 2nd | 162.6 | 205 | 27.2 | 116 574 | 26.4 | 1.2 (1.0, 1.4) |
| 3rd | 152.6 | 108 | 14.3 | 65 354 | 14.8 | 1.1 (0.9, 1.3) |
| ≥4th | 192.3 | 114 | 15.1 | 54 515 | 12.4 | 1.3 (1.1, 1.6) |
| Maternal characteristics | | | | | | |
| Age, y ^c | | | | | | |
| <17 | 265.1 | 54 | 7.1 | 18 650 | 4.2 | 1.7 (1.2, 2.3) |
| 17–19 | 167.4 | 116 | 15.2 | 64 139 | 14.4 | 1.2 (0.9, 1.5) |
| 20–24 | 153.4 | 202 | 26.4 | 121 803 | 27.4 | 1.1 (0.9, 1.3) |
| 25–29 | 146.1 | 181 | 23.7 | 114 951 | 25.8 | Referent |
| ≥30 | 156.3 | 211 | 27.6 | 125 199 | 28.2 | 1.0 (0.8, 1.2) |
| Race | | | | | | |
| White | 120.8 | 363 | 47.5 | 279 583 | 62.9 | Referent |
| Black | 238.2 | 379 | 49.6 | 145 832 | 32.8 | 1.6 (1.3, 1.8) |
| Other | 107.2 | 22 | 2.9 | 19 327 | 4.3 | 1.0 (0.6, 1.5) |
| Education, y ^e | | | | | | |
| 0–10 | 169.2 | 155 | 23.0 | 85 080 | 21.4 | 1.2 (1.0, 1.5) |
| 11–12 | 159.5 | 345 | 51.2 | 200 881 | 50.6 | 1.0 (0.9, 1.3) |
| ≥13 | 146.1 | 174 | 25.8 | 110 730 | 27.9 | Referent |
| Prenatal visits | | | | | | |
| None | 281.9 | 86 | 12.1 | 26 448 | 6.3 | 1.5 (1.1, 1.8) |
| 1–2 | 278.7 | 64 | 9.0 | 19 630 | 4.7 | 1.3 (1.0, 1.8) |
| 3–5 | 307.2 | 198 | 27.9 | 55 246 | 13.1 | 1.4 (1.2, 1.7) |
| ≥6 | 107.3 | 361 | 50.9 | 320 745 | 76.0 | Referent |
| Trimester of care | | | | | | |
| 1st | 153.8 | 476 | 66.9 | 287 414 | 67.3 | Referent |
| 2nd | 135.9 | 134 | 18.8 | 92 963 | 21.8 | 1.5 (1.0, 2.2) |
| 3rd | 72.3 | 15 | 2.1 | 19 940 | 4.7 | 1.5 (1.0, 2.3) |
| No care | 281.9 | 86 | 12.1 | 26 448 | 6.2 | 1.8 (1.1, 2.8) |
| Marital status | | | | | | |
| Married | 134.8 | 351 | 45.9 | 242 893 | 54.6 | Referent |
| Unmarried | 187.9 | 413 | 54.1 | 201 849 | 45.4 | 1.3 (1.1, 1.5) |
| Paternal characteristics | | | | | | |
| Age, y | | | | | | |
| <21 | 178.5 | 57 | 7.5 | 29 782 | 6.7 | 1.3 (1.0, 1.8) |
| 21–24 | 176.5 | 106 | 13.9 | 55 946 | 12.6 | 1.4 (1.1, 1.7) |
| ≥25 | 133.3 | 327 | 42.8 | 228 775 | 51.4 | Referent |
| Not stated | 191.7 | 274 | 35.9 | 130 239 | 29.3 | 1.3 (1.1, 1.6) |
| Education, y ^e | | | | | | |
| 0–10 | 153.1 | 75 | 16.5 | 45 539 | 16.0 | 1.0 (0.8, 1.3) |
| 11–12 | 149.7 | 234 | 51.5 | 145 776 | 51.2 | 1.0 (0.8, 1.1) |
| ≥13 | 144.6 | 145 | 31.9 | 93 533 | 32.8 | Referent |

Note. RR = relative risk; CI = confidence interval.

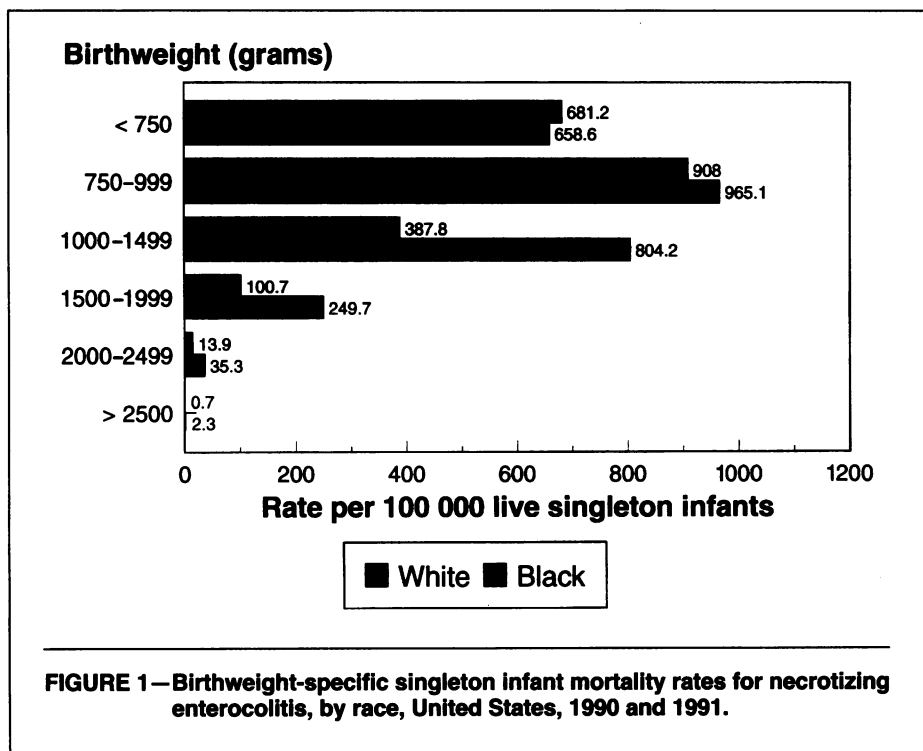
^aInfant mortality rate expressed as necrotizing enterocolitis low-birthweight singleton deaths per 100 000 live low-birthweight singleton births.

^bEstimated relative risk and 95% confidence interval for comparison of necrotizing enterocolitis deaths with surviving low-birthweight infants for infant, maternal, and paternal characteristics adjusted for birthweight. Birthweight categories used for adjusting: < 750 g, 750–999 g, 1000–1499 g, 1500–1999 g, 2000–2499 g. Birthweight-specific relative risks are reported. The reference group for which the relative risk is expressed is as indicated.

^cAdjusted relative risk estimates from multivariate logistic regression for final model as follows: birthweight (RR = 109.6; CI = 81.9; 146.8; RR = 54.7; CI = 40.9, 73.3; RR = 28.0; CI = 21.2, 37.0; RR = 7.4; CI = 5.5, 10.0); race (RR = 1.5; CI = 1.3, 1.8); sex (RR = 1.6; CI = 1.4, 1.8); and maternal age (RR = 1.5; CI = 1.1, 2.1; RR = 1.1; CI = 0.9, 1.4; RR = 1.1; CI = 0.9, 1.3; RR = 1.0; CI = 0.8, 1.2).

^dExcludes nonreporting states: California and Texas in both years; Oklahoma in 1990.

^eExcludes nonreporting states: New York and Washington.



Linked Birth/Infant Death Data

During 1990 and 1991, 1008 infants died with necrotizing enterocolitis, of whom 91% were low birthweight. Low-birthweight singleton infants accounted for 764 necrotizing enterocolitis deaths during 1990 and 1991 (Table 2). The necrotizing enterocolitis infant mortality rate for low-birthweight singleton infants (159.1 per 100 000 live low-birthweight singleton births) was significantly higher than that for singleton infants who weighed 2500 g or more at

birth (1.0 per 100 000 live normal-weight singleton births). The necrotizing enterocolitis infant mortality rates among low-birthweight infants increased with decreasing gestational age and birthweight for all low-birthweight groups, except for infants under 750 g. The rate was higher for Blacks than for Whites in each birthweight group over 750 g (Figure 1).

Low-birthweight singleton infants who died with necrotizing enterocolitis were compared with low-birthweight singleton survivors to identify risk factors for necro-

tizing enterocolitis mortality (Table 2). With birthweight taken into account, the risk of necrotizing enterocolitis death was significantly greater for Black infants than for White infants, and the risk was significantly higher for male infants than for female infants. This increased risk was also associated with decreased gestational period and a lower 1-minute Apgar score (<8). When the infant's birthweight was taken into account, the risk of necrotizing enterocolitis death was higher for infants born to Black mothers, unmarried women, mothers younger than 17, and those having fewer or no visits for prenatal care (Table 2). The risk was unrelated to parental education, but was higher for infants born to fathers younger than 25 years of age and age unrecorded. When multiple logistic regression was used, the variables that remained associated with necrotizing enterocolitis death, in addition to low birthweight, included race, sex, and mother's age group (Table 2). When gestational period was included in the model, the results were similar.

Two thirds (69%) of low-birthweight singleton deaths from all causes occurred in the first week of life, but only 14% of low-birthweight singleton necrotizing enterocolitis deaths occurred in the first week (Table 3). The majority (70%) of low-birthweight singleton necrotizing enterocolitis deaths occurred from 7 through 27 days of life. For these low-birthweight preterm infants, age at death was inversely related to birthweight. The lightest, most immature infants were least likely to die with necrotizing enterocolitis during the first week of life and most likely to die in the postneo-

TABLE 3—Age at Death from Necrotizing Enterocolitis and All Causes by Birthweight and Race for Low-Birthweight Singleton Infants: United States, 1990 and 1991^a

| Birthweight, g | All Infants, Age at Death | | | White Infants, Age at Death | | | Black Infants, Age at Death | | |
|--|---------------------------|--------------------|-----------------------------|-----------------------------|--------------------|-----------------------------|-----------------------------|--------------------|-----------------------------|
| | 0-6 Days, No. (%) | 7-27 Days, No. (%) | 28 Days to <1 Year, No. (%) | 0-6 Days, No. (%) | 7-27 Days, No. (%) | 28 Days to <1 Year, No. (%) | 0-6 Days, No. (%) | 7-27 Days, No. (%) | 28 Days to <1 Year, No. (%) |
| Necrotizing enterocolitis^a | | | | | | | | | |
| <750 | 9 (5.4) | 121 (72.0) | 38 (22.6) | 5 (5.8) | 62 (72.1) | 19 (22.1) | 4 (5.6) | 50 (69.4) | 18 (25.0) |
| 750-999 | 5 (3.0) | 122 (73.9) | 38 (23.0) | 3 (3.3) | 71 (78.0) | 17 (18.7) | 2 (2.8) | 49 (69.0) | 20 (28.2) |
| 1000-1499 | 24 (10.1) | 186 (78.2) | 28 (11.8) | 11 (11.5) | 75 (78.1) | 10 (10.4) | 12 (9.1) | 102 (77.3) | 18 (13.6) |
| 1500-1999 | 41 (31.5) | 77 (59.2) | 12 (9.2) | 15 (28.9) | 32 (61.5) | 5 (9.6) | 25 (32.9) | 44 (57.9) | 7 (9.2) |
| 2000-2499 | 28 (44.4) | 26 (41.3) | 9 (14.3) | 11 (40.7) | 13 (48.2) | 3 (11.1) | 17 (48.6) | 13 (37.1) | 5 (14.3) |
| Total | 107 (14.0) | 532 (69.6) | 125 (16.4) | 45 (12.8) | 253 (71.9) | 54 (15.3) | 60 (15.5) | 258 (66.8) | 68 (17.6) |
| All causes | | | | | | | | | |
| <750 | 15216 (88.0) | 1045 (6.0) | 1028 (6.0) | 8052 (89.1) | 517 (5.7) | 470 (5.2) | 6689 (86.9) | 489 (6.4) | 517 (6.7) |
| 750-999 | 2718 (62.2) | 749 (17.2) | 900 (20.6) | 1722 (66.2) | 462 (17.8) | 419 (16.1) | 893 (55.5) | 260 (16.2) | 455 (28.3) |
| 1000-1499 | 2321 (55.5) | 724 (17.3) | 1137 (27.2) | 1612 (61.6) | 422 (16.1) | 583 (22.3) | 608 (43.5) | 273 (19.5) | 517 (40.0) |
| 1500-1999 | 2025 (50.8) | 537 (13.5) | 1425 (35.7) | 1480 (56.2) | 341 (13.0) | 811 (30.8) | 451 (38.8) | 170 (14.6) | 542 (46.6) |
| 2000-2499 | 2060 (36.6) | 773 (13.7) | 2800 (49.7) | 1501 (41.4) | 499 (13.8) | 1630 (44.9) | 462 (26.4) | 235 (13.4) | 1056 (60.2) |
| Total | 24340 (68.6) | 3828 (10.8) | 7290 (20.6) | 14367 (70.0) | 2241 (10.9) | 3913 (19.1) | 9103 (66.9) | 1427 (10.5) | 3087 (22.7) |

^aNecrotizing enterocolitis accounted for 1.4% of White low-birthweight neonatal singleton deaths and 2.5% of Black low-birthweight neonatal singleton deaths.

natal period. Low-birthweight Black neonates who weighed less than 750 g were significantly less likely to die from all causes in the first week of life than were White neonates. In contrast, there was no difference in the timing of necrotizing enterocolitis deaths by race.

Discussion

Necrotizing enterocolitis in the United States remains an important cause of neonatal morbidity and mortality, especially among low-birthweight preterm infants. Both incidence rates and case-fatality rates increase with decreasing birthweight and gestational age.¹ Neonatal and postneonatal infant mortality rates have declined in the past decade.⁶ The improvement in survival, particularly after 1989, has been partly linked to the introduction and widespread use of exogenous surfactants.⁷ The present study used national death and birth cohort data to describe recent trends in necrotizing enterocolitis mortality, to compare necrotizing enterocolitis mortality rates in the pre- and post-surfactant eras, and to evaluate risk factors for necrotizing enterocolitis deaths.

Necrotizing enterocolitis infant mortality rates decreased from 1979 through 1985, a decrease that was attributed to improved neonatal care.⁵ However, necrotizing enterocolitis mortality rates appear to have increased since 1986, a time when overall neonatal and postneonatal mortality rates have declined in the United States.⁶ In the early 1990s, necrotizing enterocolitis was more commonly associated with extreme prematurity than in the 1980s. Most necrotizing enterocolitis deaths occurred after 1 week of age (i.e., in infants who survived early causes of mortality). These data suggest that improvements in survival of smaller, more immature infants—those at greatest risk for necrotizing enterocolitis—may be accompanied by a further increase in necrotizing enterocolitis-associated infant mortality. As the medical and surgical care of sick newborns has improved, necrotizing enterocolitis case-fatality rates have been reduced.¹ Therefore, the increase in necrotizing enterocolitis infant mortality rates reported here suggests an even larger increase in the number of necrotizing enterocolitis cases. Intervention strategies to reduce the incidence of this serious complication of prematurity are needed.

Necrotizing enterocolitis infant mortality rates were highest for Blacks, and necrotizing enterocolitis deaths among Blacks increased in the early 1990s. Previous studies attributed this racial difference

to the increased incidence of prematurity among Black infants.^{5,28} However, the racial difference remained statistically significant even after birthweight and other characteristics were controlled for. These data, which are consistent with a significantly increased risk for infant mortality reported among Black infants,^{29,30} highlight the disparity in health outcomes between Blacks and Whites and deserve further study. A partial explanation may lie in the difference in the timing of deaths from all causes among White and Black low-birthweight infants. Low-birthweight Black neonates, especially those weighing less than 750 g, were significantly less likely to die in the first week of life than White neonates, suggesting that more low-birthweight Black infants survive to make up the premature cohort at risk for necrotizing enterocolitis.

While no consistent association has been found between sex and the incidence of necrotizing enterocolitis,¹ male low-birthweight singleton infants were at a higher risk for necrotizing enterocolitis death, even after adjustments for birthweight and other characteristics. The increased rate for males may reflect the higher birthweight-specific infant mortality rates among males overall.²⁹

The highest necrotizing enterocolitis infant mortality rate and the greatest proportion of necrotizing enterocolitis infant deaths occurred in the South, paralleling an increase in infant mortality from all causes in the South. This finding may be explained by an increased rate for Black and preterm births in the South.³¹

Prematurity and low birthweight were most commonly associated with necrotizing enterocolitis mortality. Strategies to decrease the incidence of prematurity may have the greatest impact on reducing the number of necrotizing enterocolitis cases and necrotizing enterocolitis mortality. In fact, countries with low rates of prematurity have low rates of necrotizing enterocolitis.³² However, the rate of preterm births in the United States has risen in recent years.^{33,34} These findings underscore the need for a national agenda to decrease the incidence of premature births. □

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